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AMERICAN JOURNAL OF PHARMACY

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CONTENTS

E D I T O R I A L

THE NEED FOR A STANDARDIZED INTERNSHIP IN PHARMACY

ONE of the most troublesome technicalities plaguing the graduate in pharmacy is the lack of uniformity in the internship—sometimes called apprenticeship—specified in various states to fulfill their practical experience requirement in order to qualify for licensure. It seems that almost every state has a different idea as to when and how experience should be counted. Some states, for example, credit experience gained long before a young man has even entered a college of pharmacy. It seems quite obvious that such experience is of very doubtful value and, as a further evil, many persons obtain apprentice certificates who never intend to study pharmacy and use them only as a subterfuge to do semiprofessional work in the prescription department. Other states give credit for some of the total experience required on the basis of work in a pharmacy while enrolled in a college of pharmacy. Still others credit only the time during which the student is not actually in college; i.e., summer vacations. At least one state gives credit only for experience gained *after* graduation from college and, in this particular state, a full year's internship is required following graduation. For a long time, it has been a fairly well-established principle that a registered pharmacist who wished to register in another state by reciprocity must, at the time of his initial registration in the first state, have met the requirements in the state in which he wishes to register. This seems like a perfectly reasonable requirement since a board could not very well register by reciprocity someone who did not meet their own standard when he first was registered.

The time has come, however, when the entire matter of practical experience should be subjected to an honest and unprejudiced appraisal, and clear-cut decisions made based on objective logic. This need will be made even more acute with the adoption of the five year program in pharmacy. While we do not question the value of drugstore experience to the pharmacy student, we do wish to challenge crediting such experience for state board purposes. No student can

properly appreciate the professional work in a pharmacy until he has completed his professional courses in college and the great bulk of these, as might be expected, is found in the last year of his college work. As a result, much of the so-called experience gained in the pharmacy during the summer vacations is of somewhat doubtful quality. The logical time for this experience to be obtained is after graduation from college and not "sandwiched" between the years of college attendance. A few months of experience after college graduation is many times more meaningful than several times this much experience obtained before the proper foundation is obtained.

There are many more reasons well-known to pharmaceutical educators why the present practice of giving credit for work before graduation should be abandoned. Many pharmacists, realizing that the student must have this experience credit to qualify for the board, uses this as a means of exploiting the young person and even subjecting him to coercion. The pharmacy student is often paid far less than a bus boy at the soda fountain or luncheonette and is often forced to work even while going to college as a means of keeping his position open for the summer. As a result, many students put in far too many hours working while in college and thereby detract from their scholastic achievement, sometimes to the point of failure. It frequently happens that a student at the end of a school year is in poor physical condition and needs more than anything else a summer spent out of doors as a means of improving his health and vitality. The constant spectre of not fulfilling his experience requirement forces him to take employment in a pharmacy even though it is a serious threat to his health and may jeopardize his fitness to return to college in the fall.

It is high time that the profession of pharmacy cast off the antiquated practice and philosophy of apprenticeship. This dates back to the time when it was by apprenticeship only that the pharmacist received his training and, by today's standards, it is an anachronism. Thus, we argue that it is time for our boards of pharmacy in every state to take a new, hard look at this problem. We still believe in the importance of practical experience but, insofar as meeting board requirements is concerned, we recommend the following:

1. That the practical experience required by our boards be in the form of an internship program.

2. That no credit be given for experience gained prior to graduation from college.

3. That a uniform requirement of no more than six months' practical experience after graduation from college be adopted by all states.

4. That immediate steps be taken in each of the states to so amend the Pharmacy Act or the regulations of the board of pharmacy to make this possible.

5. That the National Association of Boards of Pharmacy use its influence to stimulate and bring about the acceptance of this program as one which is urgently needed.

As a final closing comment, all of us must realize that the present confusion works a hardship and will continue to work a hardship on those who are completely powerless to alter the situation; namely, our present students and those who will come after them. Some definite action on this matter is long overdue.

L. F. Tice

A STUDY OF THE LYOPHILIZATION OF CARBOPOL 934 [1]

By Mahesh S. Mehta [2] and W. Lewis Nobles [3]

CARBOPOL 934 [4] is a finely divided, free-flowing, acid polymer which readily disperses in water to yield a solution possessing an acid pH with a low viscosity. Neutralization of the acid polymer with an appropriate alkaline substance (sodium hydroxide, sodium carbonate, or triethanolamine) results in a stable gel with increased viscosity characteristics. These neutralized solutions of Carbopol are resistant to bacterial or fungal attack. This gives the Carbopol suspension a distinct advantage over most natural gums and other similar products.

Gums and other suspending agents are commonly employed by pharmaceutical manufacturers and retail pharmacists for various formulations and prescription compounding. These hydrophilic materials may exhibit a slow rate of solution or dispersion and, on occasion, long periods of heating, stirring and/or specialized techniques are needed to accomplish dispersion or solution. Previous reports (1) indicated that certain gums and other suspending agents are readily soluble in their lyophilized form and this treatment decreased the time and effort required to prepare emulsions, lotions, and similar preparations. Consequently, the present investigation was undertaken in an effort to determine the effect of lyophilization on the rate of solution or dispersion of Carbopol 934. In addition, studies were carried out on a number of suspensions of commonly used pharmaceuticals, utilizing Carbopol 934, to determine the effect of lyophilization of the suspending agent on these preparations.

Experimental

In order to determine whether there is any change in the rate of solution, pH, viscosity and suspending properties of the lyophilized Carbopol 934 as compared with the original, a one per cent solution of this agent was prepared (2) and lyophilized using a modified Campbell-Pressman unit (3).

[1] This project was supported in part by a grant-in-aid from the B. F. Goodrich Chemical Company, Cleveland, Ohio.

[2] Present address: Mehta Street, Rajpipla (Bombay State) India.

[3] Professor of Pharmacy and Pharmaceutical Chemistry, University of Mississippi, University, Mississippi. Present address: c/o College of Pharmacy, University of Michigan, Ann Arbor, Michigan.

[4] A product of B. F. Goodrich Chemical Company.

Procedure

1. *Lyophilization of the Solutions and Suspensions.*—The lyophilizer was prepared for freeze-drying as indicated by the manufacturer (3). The condenser, freezing trap and freezing pans were all first frozen with acetone and dry ice. Twenty-five grams of the sample was weighed in each flask and subjected to dry ice-acetone treatment for thirty minutes. After this period of time, the lyophilizer was attached to a vacuum pump and the material allowed to remain on the lyophilizer for thirty-six hours. At the end of drying, the pump was stopped and the vacuum was disconnected. The flasks were taken from the apparatus, cleaned from the outside, weighed, and then placed in the desiccator for overnight drying. After desiccation, the flasks were again weighed, and the percentages of solids obtained were calculated. The dry solids were scraped off from the flasks and were stored in well-closed containers. This dry powder was used for subsequent tests.

2. *Reconstitution.*—Approximately one-half the weight of the dry solids obtained was weighed and enough water added to make up to the desired volume or weight. The suspensions were reconstituted by triturating in a mortar.

3. *pH.*—The pH of the reconstituted sample was taken immediately after reconstitution. The pH of an original sample was taken at approximately the same time, both determinations being made on a Beckman Model G pH Meter. These readings were repeated at one and four week intervals. (See Table I.)

TABLE I

pH AND VISCOSITY

Sample	pH Fresh	pH After 1 week	pH After 4 weeks	Viscosity
Original	6.75	6.3	6.2	68,000 cps
Lyophilized	6.8	6.3	6.1	14,000 cps

Lyophilization time—36 hours
% of Solids—1.2%
Physical characteristics—Thin papery gelatin-like material.

4. *Viscosity.*—The viscosity determinations was made using a Beckman synchro-lectric viscometer (multi-speed model LVF). These measurements were made on the reconstituted sample immediately after reconstitution and on the original immediately after the completion of the preparation.

5. *Suspending Properties.*—Ten insoluble substances (see Table II) were suspended in different concentrations of Carbopol 934 and corresponding concentrations of the recently lyophilized material.

6. *Preparation of the Suspensions.*—The insoluble substance was weighed and placed in a mortar, triturated with 3 ml. of glycerin and the Carbopol solution added as the suspending agent. This mixture was triturated well and water added slowly with trituration to make the volume up to 100 ml. Each sample was placed in a 100 ml. flask and compared after 120 hours with another suspension made with the original Carbopol solution which had been set aside for the same time interval. Both samples were examined for percentage of settling and characteristics of the suspensions after 120 hours.

Discussion of Results

The lyophilized material was converted into a smooth gel immediately upon the addition of water without the necessity of agitating in any manner. During a period of storage of three months, there was no change in the physical appearance of the lyophilized material.

The data in Table I reveal that there is practically no difference in the pH due to lyophilization immediately after reconstitution and after an interval of four weeks. Also from Table I, it may be noted that there was a marked decrease in the viscosity of the gel prepared with the lyophilized material as compared with the original.

From Table II, it is seen that in the 20% concentration there was practically no difference in either type of suspension, while with the 40% concentration there was some difference observed with certain ingredients in the two types of suspensions. Kaolin and ichthammol were satisfactorily suspended with both concentrations of the lyophilized material and the original sample. With the 40% concentration of lyophilized material, there was observed a marked decrease in the stability of the suspensions of sulfanilamide and coal tar. Gantrisin ®, bismuth subnitrate, magnesium oxide, magnesium carbonate and calcium carbonate were poorly suspended with both concentrations of

TABLE II

A Comparison of Suspensions Utilizing 1% Carbofol 934 at pH 7 with Lyophilized Samples

Observation after 120 hrs. Ingredient + 3% Glycerin + Suspending Agent + Water q.s. 100 ml.	With 20% w/w of Carbopol 1% Solution Original	Lyophilized	With 40% w/w of Carbopol 1% Solution Original	Lyophilized
1 Gantrisin [1] 5%	85% separation. Poor. Flaky.	85% separation. Poor. Flaky.	76% separation. Poor. Flaky.	77% separation. Poor. Flaky.
2 Sulfanilamide 5%	90% separation. Poor.	91% separation. Crystal growth.	No separation. Good. Thick but pourable.	86% separation. Poor. Granular.
3 Kaolin 10%	13% separation. Good.	8.5% separation. Good.	No separation. Good. Thick but pourable.	Good. 2% separation.
4 Bismuth subnitrate 5%	75% separation. Poor. Granular	68% separation. Poor.	70% separation. Poor cake.	57% separation. Poor. Granular.
5 Sulfur ppt. 5%	81% separation. Poor. Flaky.	84% separation. Poor. Flaky.	No separation. Good. Thick but pourable.	52% separation. Poor. Granular.
6 Ichthammol 10%	No separation. Good.	No separation. Good. Bright.	No separation. Good.	No separation. Good.
7 Magnesium oxide 5%	25% separation. Poor. Granular-cake.	46% separation. Poor. Smooth cake.	13% separation. Poor. Granular cake.	4% separation. Poor cake.
8 Magnesium carbonate 5%	36% separation. Poor granular cake.	40% separation. Poor smooth cake.	52% separation. Poor granular cake.	30% separation. Poor cake.
9 Calcium carbonate 5%	66% separation. Poor.	41% separation. Poor.	53% separation. Poor.	25% separation. Poor. Granular.
10 Coal Tar 5%	3% separation. Good.	59% separation. Poor.	No separation. Good. Thick.	Poor. 25% separation.

[1] Brand of sulfisoxazole, Hoffmann & La Roche, Nutley, N. J.

original and lyophilized ones. One interesting phenomenon which was observed was that most of the preparations made with the lyophilized material were much smoother than those made with the original.

Conclusions

(1) The lyophilization of Carbopol is feasible and the rate of solution is markedly increased.

(2) The lyophilized material is obtained at the same pH at which it was lyophilized and no appreciable change in the pH during a period of four weeks was noted.

(3) There is a marked decrease in viscosity due to lyophilization.

(4) The suspending property is not decreased commensurate with the decrease in viscosity.

REFERENCES

(1) Lachman, Leon and Chavkin, Leonard, *J. Amer. Pharm. Assoc., Sci. Ed., 46,* 412 (1957).

(2) Goodrich Service Bulletin (G-20) dealing with Carbopol 934.

(3) Brochure "Freeze-Drying Apparatus" by E. Machlett & Sons, New York, New York.

LEUCOMYCIN—A NEW ANTIBIOTIC

By E. A. Pachtman, J. M. Beiler, and Gustav J. Martin *

LEUCOMYCIN is an antibiotic derived from *Streptomyces Kitasatoensis*. It was purified and characterized by Sano (1). Chemically, Leucomycin is related to erythromycin and carbomycin, and its main activity is against Gram positive organisms. The ready development of resistance among streptococci and staphylococci, and the relative dearth of antibiotics affecting these organisms suggested that Leucomycin might be of considerable clinical utility. An investigation was therefore undertaken to confirm and extend the Japanese reports.

Experimental

The *in vitro* work was done turbidimetrically. Organisms were grown in Trypticase Soy Broth, and determinations made after 24 hour incubation. The *in vivo* work was done in mice. Infecting organisms were injected intraperitoneally except in the case of Influenza PR-8 virus, which was given intranasally. Antibiotics were given intraperitoneally in three doses: immediately following infection, four hours after, and eight hours after.

Results

Results obtained in *in vitro* testing are shown in Table I. Leucomycin appeared, as had been reported (1), to be mainly effective against Gram positive organisms; quantitatively, its effects compared favorably with those of other antibiotics, such as erythromycin and carbomycin, with the same spectrum.

This was confirmed, as far as spectrum and activity are concerned, by *in vivo* testing. Leucomycin was inactive against the Gram negative organisms used (Table II), as were penicillin and erythromycin. Results are averages for ten animals in each group. With Gram positive organisms, however, definite activity was manifested (Table

* Research Laboratories, The National Drug Company, Philadelphia 44, Pennsylvania.

III). Against Influenza PR-8 and Col. SK viruses Leucomycin, as well as the other antibiotics tested, showed no activity.

In vivo, therefore, Leucomycin is an effective agent for treatment of infections produced by Gram positive organisms. Its activity compares favorably with that of the antibiotics to which it was compared.

TABLE I

IN VITRO EFFECTS OF LEUCOMYCIN

Organisms	*Effective Concentration (mcg./ml.)*
Strep. hem.	2.5
Staph. aureus	2.0
E. coli	Neg.
Shig. dysent.	5.0
Ps. aeruginosa	10.0
Sal. typhosa	Neg.
M. tuberculosis	Neg.

TABLE II

ACTION OF LEUCOMYCIN ON GRAM NEGATIVE ORGANISMS IN VIVO

Antibiotic	*Dose (mcg/animal)*	*Ps. aeruginosa*		*E. coli*	
		Av. survival time (hrs.)	*% Survivors*	*Av. survival time (hrs.)*	*% Survivors*
Leucomycin	500	24	0	24	0
"	125	24	0	24	0
Streptomycin	500	24	10	>24	70
"	125	24	30	>24	50
Penicillin	500	24	10	24	0
"	125	24	0	24	0
Erythromycin	500	24	0	24	0
"	125	24	0	24	0
Control	—	24	30	24	0

TABLE III

EFFECT OF LEUCOMYCIN ON GRAM POSITIVE ORGANISMS

Antibiotic	*Dose (mcg/animal)*	*D. Pneumoniae*		*Strep. hemolyticus*		*Staph. aureus*	
		Survival time (days)	*% Survivors*	*Survival time (days)*	*% Survivors*	*Survival time (hrs.)*	*% Survivors*
Leucomycin	30	>4.3	40	—	80	>43	50
Leucomycin	60	>3.7	70	—	80	>54	40
Leucocymin	120	—	90	—	90	—	80
Leucomycin	240	—	100	—	—	—	—
Erythromycin	30	3.6	10	—	60	—	100
Erythromycin	60	4.2	0	—	90	—	100
Penicillin	25	2.0	10	1.1	0	—	100
Penicillin	50	2.0	20	1.0	0	—	100
Streptomycin	50	1.8	0	3.6	10	—	100
Streptomycin	100	2.0	0	3.8	10	—	100
Control	—	1.0	30	1.0	0	18	30

BIBLIOGRAPHY

(1) Sano, Y., *J. Antibiotics 1,* 93 (1954).

DRUG INFORMATION SOURCES*

(Canada, Great Britain, The Netherlands and the United States)

Supplemental Data

CANADA

The following entries supplement the list in *American Journal of Pharmacy* 129:9-10 (January 1957):

Drug Index 1958. (Part 2, Oct. 15, 1957, issue of Drug Merchandising). 106 pp. Publisher's address: Maclean-Hunter Publishing Co., Ltd., 481 University Avenue, Toronto 2, Canada.

New Products Index.

Volume 13, covering specialties marketed in Canada to May 1, 1958, incorporates a change from the pocket size formerly used to the full size of *The Canadian Pharmaceutical Journal.* The index by manufacturers has been omitted from this volume. It is supplemented by monographs on new drugs published in the monthly issues of the *Journal.* The *Journal* is also reprinting monographs from volume 8, which is now out of print. Publisher's address: 221 Victoria Street, Toronto, Ontario.

Trade Marks and Trade Names Registered With the Canadian Pharmaceutical Manufacturers' Association. Toronto, The Association, 1954. 90 pp.

An alphabetic list of trade names of the members of the Association, giving name of firm and date of use. A cumulative supplement is issued semiannually. Publisher's address: King Edward Sheraton Hotel, Toronto 1.

V-1; Vademecum International. 1958. 1957. $1.60. Publisher's address: Montreal 8, Canada.

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*A World List; compiled by the Pharmaceutical Section, Science-Technology Division, Special Libraries Association.

GREAT BRITAIN

The following entries supplement the list in *American Journal of Pharmacy* 129:95-98 (March 1957):

The British Encyclopaedia of Medical Practice. Pharmacopoeia. 2nd ed. London, Butterworth & Co., 1957.

An extensive compilation of monographs on therapeutic and diagnostic agents. Monographs are entered under proprietary names and provide name of manufacturer, composition, actions, indications, dosage and method of administration, contraindications and possible side effects and forms and sizes supplied. Information is included for more than 1400 products. A therapeutic index is also included. Addresses of all overseas representatives are listed, as well as domestic addresses of manufacturing firms. Publisher's address: 88 Kingsway, London, W. C. 2.

"The Compend"; Addendum for the year 1956, compiled by William Hetherington. 1957. 58 pp. Publisher's address: Bath Road, Bristol 4, Eng.

Guide to New Medicaments. London, **The Chemist and Druggist.**

Gummed reprints of the monthly "Guide to New Medicaments" feature of *The Chemist and Druggist* are issued free to subscribers to the periodical. Each entry, a monograph on a newly released drug, reports name and address of manufacturer, composition, indications, dosage, how supplied, date product was issued and sometimes literature references. Cross references to alternate names are also provided. The subscription price of the journal is £2 10s. Publisher's address: 28 Essex Street, Strand, London, W. C. 2.

The London Medical Handbook. London, British and Colonial Druggist. Annual, 10s./6d.

An extensive annual list of medical specialties sold in Great Britain. Entries are alphabetic by proprietary name and provide name and address of manufacturer and brief statements of composition and indications. A therapeutic index is also included. Publisher's address: 194-200, Bishopsgate, London, E. C. 2.

New Prescription Products. London, **The Alchemist.** Cards 3″ by 5″.

Information about the prescription products released in the United Kingdom is published in a card-index supplement to *The Alchemist.* Entries are under proprietary names and provide name of manufacturer, composition, indications, dosage, packings and prices and restrictions on sale, if any. Minor amendments to supplements are published in *The Alchemist.* Classified lists of the products referred to in the Supplement are also published from time to time in *The Alchemist.* The annual subscription, including the Supplement, is 20s. Publisher's address: 25 Oxford Street, London W. 1.

Pharmaceutical Society of Great Britain. British Pharmaceutical Codex 1954: Supplement 1957. 1957. 124 pp. 27s. 6d.

New and revised monographs relating to substances included in *Addendum 1955* to *British Pharmacopoeia* and amendments published in *Pharmaceutical Journal* since the *British Pharmaceutical Codex* was issued. Publisher's address: Pharmaceutical Press, 17 Bloomsbury Square, London, W. C. 1.

Pharmaceutical Society of Great Britain. The Extra Pharmacopoeia (Martindale), incorporating Squire's Companion. 24th ed. Vol. 1. 1958. 1695 pp. 65s.

Main titles of drugs are given in English instead of Latin. Information from foreign pharmacopoeias and information about specialties have both been expanded. Specialties are listed at the end of the subsection relating to the principal ingredient and details of composition and dosage are given. Publisher's address: Pharmaceutical Press, 17 Bloomsbury Square, London W. C. 1.

NETHERLANDS

The following entries supplement the list in *American Journal of Pharmacy* 129:98-101 (March 1957):

Geneeskundig Jaarboekje voor Nederland, edited by Dr. S. A. Westra and J. B. Lenstra. 75th year. Rotterdam, Van Hengel, 1958. 399 pp. Hfl. 12.50.

This yearbook contains an extensive alphabetic list of drugs, including both common drugs and specialties. For each is given brief

composition, indications and dosage, but no manufacturer. Separate sections list hormones, vitamins and vaccines. A section describing poisons and their antidotes is also included. Publisher's address: Schiedamsevest 51, Rotterdam-2.

Pharmacological and Chemical Synonyms, compiled by E. E. J. Marler. 2nd ed. Amsterdam, **Excerpta Medica,** 1958. 175 pp. Hfl. 19.—; $5.00.

The new edition lists approximately 8000 synonyms of drugs collected from the medical literature of the world. It is expected to be revised at approximately 2-year intervals. A discount is offered to *Excerpta Medica* subscribers. Publisher's address: 111 Kalverstraat, Amsterdam and 2 East 103rd Street, New York 29, N. Y., U. S. A.

Side Effects of Drugs, compiled by L. Meyler, M.D. Amsterdam, The Excerpta Medica Foundation, 1957 to date.

An annual survey of the medical literature of the world for reports of untoward effects of drugs. Drugs are grouped in chapters according to pharmacologic action and appear in bold-face type under their generic names. Synonyms, including chemical and proprietary names follow the generic names. Side effects are reported in detail and each report is documented by reference to the medical literature. A general alphabetic index to all names and to classes of drugs is presented. Volume 1, covering the literature of 1955-1956, is $3.95 and Volume 2, for 1957, $5.00. Publisher's address: 111 Kalverstrasse, Amsterdam, and 2 East 103rd Street, New York, N. Y., U. S. A.

Therapie Compendium; Receptuur voor de Huisarts, by Henri R. M. de Haan. 7th ed. Leiden, L. Stafleu, 1958.

A physician's handbook of drugs and other therapeutic measures for the treatment of diseases. Diseases are entered alphabetically. Monographs include, besides description of disease state and therapeutic measures, formulas for compounding preparations, dosages and precautions to be observed. Lists of specialties are frequently included with brief indication of components. There is an alphabetic index to common names and one for proprietary names, the latter giving name of manufacturer. Publisher's address: Stationsweg 10, Leiden.

UNITED STATES

The following entries supplement the list in *American Journal of Pharmacy* 129:5-9 (January 1957):

Accepted Dental Remedies; Drugs Used in Dental Practice Including a List of Brands Accepted by the Council on Dental Therapeutics of the American Dental Association. 23rd ed. American Dental Association, 1958. 214 pp. $3.00.

The new edition represents a marked revision in organization and content. Greater emphasis is placed on the significance of drugs currently and frequently administered in medical practice in order to alert the dentist to the complications which may arise when the patient is receiving medical care at the time dental treatment is provided. Publisher's address: 222 East Superior Street, Chicago 11, Illinois.

American Drug Index 1958. Lippincott, 1958. 716 pp. $5.00. Publisher's address: East Washington Square, Philadelphia 5, Pennsylvania.

American Medical Association. Council on Drugs. New and Nonofficial Drugs, 1958. Lippincott, 1958. 645 pp. $3.35.

Monographs in this edition give available dosage forms, as well as manufacturer's brand names. Publisher's address: East Washington Square, Philadelphia 5, Pennsylvania.

1958-1959 Blue Book. 1958. 702 pp. $9.00. Publisher's address: American Druggist, 250 West 55th Street, New York 19, New York.

Drug Topics Red Book. 1958 edition. 1957. 630 pp. $9.00. Publisher's address: Topics Publishing Co., 10 East 15th Street, New York 3, New York.

Drugs of Choice, 1958-1959, by Walter Modell. St. Louis, C. V. Mosby, 1958. 931 pp. $12.75.

In this first volume of a new series, chapters are devoted to clinical disease states and the use of drugs in the conditions named is critically evaluated. The author describes the clinical condition, dis-

cusses the action of the several drugs used and reviews the data which make one or another the "drug of choice" in a specific condition. He adds his views of what the future holds and what is lacking in drug therapy in the particular area. Each section has a list of selected references which provided the data on which the opinions expressed are based. If a drug has more than one action, it may be considered in more than one section. Drug mixtures are not often considered, nor are biologicals included. Following each chapter is an extensive but not necessarily complete *Drug Index,* which lists drugs commonly used for the disturbances under consideration, including for each a brief statement of composition, dosage forms available and, as far as practical, proprietary names and manufacturers. The general alphabetic index includes proprietary, generic and common names. Publisher's address: 3207 Washington Blvd., St. Louis 3, Mo.

Modern Drug Encyclopedia and Therapeutic Index. 7th ed., ed. by Edwin P. Jordan. New York, Drug Publications, 1958. 1516 pp. $17.50 including supplements.

Products of 300 companies are listed. Biological preparations and allergens have been combined alphabetically with pharmaceuticals. Indications of narcotic status have been expanded in accordance with new regulations. Publisher's address: 11 East 36th Street, New York 16, N. Y.

Physicians' Desk Reference to Pharmaceutical Specialties and Biologicals 1958. 12th ed. 1957.

A supplement is published in May. Publisher's address: 550 Kinderkamack Road, Oradell, N. J.

Trade-Marks Registered With the American Drug Manufacturers Association and American Pharmaceutical Manufacturers' Association. Washington, D. C., Combined Trademark Bureau, 1957. 104 pp. $12.50.

—Cumulative Monthly Supplement, $15.00 per year.

This list contains trade marks and generic names currently being used in the United States and Canada by members of the two associations for their products. With each entry is a numeric reference to the manufacturer and a reference to the weekly *Bulletin* of the

Combined Trade-mark Bureau in which the mark or name appeared. A list of manufacturers with their addresses is included. It is kept up-to-date by the *Cumulative Monthly Supplement*. Publisher's address: Pharmaceutical Manufacturers Association (the associations were merged in 1958), 503-7 Albee Building, Washington 5, D. C.

Veterinary Drug Encyclopedia and Therapeutic Index. 6th ed., edited by H. C. Stephensen and S. G. Mittelstaedt. 1958. 412 pp. $7.00.

New sections have been added for cat and dog foods and feed additives. Publisher's address: 11 East 36th Street, New York 16, N. Y.

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CHEMOTHERAPY OF 624 CASES OF HODGKIN'S DISEASE WITH MISCELLANEOUS AGENTS

By John R. Sampey, Ph.D.*

IN a recent study, five chemical agents; namely, nitrogen mustards, TEM, antibiotics, ACTH/cortisone, and colchicines, were employed in the management of 4837 cases of Hodgkin's disease (H. D.).[1] In the present paper, more than 50 chemical agents have been tested in 624 patients with H. D. The number of cases with any single agent is too limited to have statistical significance, but the results do have value as a world-wide screening program for possible agents of use in the management of this tragic malignant disease. From the sources of the references, it will be seen that most of the research was done in medical centers outside of the U. S.

Results of the clinical trials with the eight most frequently used chemicals are tabulated in Table I. More detailed information on all is presented in Table II. The original medical literature has been made available by the National Library of Medicine, and the libraries of Furman University and the Greenville General Hospital.

TABLE I

THERAPY OF H. D. WITH EIGHT CHEMICAL AGENTS

Agents	*No. of Refs.*	*No. of Cases*	*No. of Remissions*	*Remission Rates*
Myleran	6	63	41	77% [2]
Phenylbutazone	7	61	42	69%
Phosphoramides	12	41	27	66%
Radiophosphorus	12	35	18	51%
FAA	12	34	5	14%
Urethan	6	33	4	12%
Ethyleneimines	8	24	17	71%
Radioarsenic	7	12	11	92%

* Furman University, Greenville, South Carolina.

[1] Sampey, J. R., *Am. J. Pharm. 128*, 271-9 (1956).

[2] Ten cases with myleran were in a reference which did not give the number of remissions observed.

TABLE II

THERAPY OF H.D. WITH MISCELLANEOUS AGENTS

No. of Cases	*No. Responding*	*Comments on Therapy*	*References*
1	1	Phosphoramides. Good response.	Bernard 1953
1	1	Phosphoramides. Remission for 27 weeks.	Farber 1953
—	—	Phosphoramides. Good remissions.	Hunter 1956
18	11	Phosphoramides. 6 Complete, 5 partial remissions.	Leonard 1956
3	1	Phosphoramides. Fair response.	Shay 1953
1	1	Phosphoramides. Brief remission.	Smith 1955
1	1	Phosphoramides. Subjective improvement 2 weeks.	Sykes 1953
4	3	Phosphoramides. 1 Good, 2 fair objective rems.	Sykes 1953
2	2	Phosphoramides. Some remissions.	Winkler 1956
—	—	Phosphoramides. Some remissions.	Wright 1953
5	3	Phosphoramides. Partial remissions.	Wright 1955
5	3	Phosphoramides. 1 Complete rem. 2 yrs., 2 brief rems.	Wright 1957
1	1	P^{32}. Brief remission.	Boltanshi 1954
7	—	P^{32}. No response.	Cooper 1951
12	10	P^{32}. Good objective rems. in 5, fair in 5.	Ferrini 1957
6	1	P^{32}. Good remission.	Guerin 1955
—	—	P^{32}. Little response.	Heilmeyer 1955
1	1	P^{32}. Patient returned to work after 6 months.	Herve 1949
5	4	P^{32}. Good remissions.	Huguenin 1951
—	—	P^{32}. Some response.	Marchal 1952
3	1	P^{32}. Brief remission.	Romieu 1953
—	—	P^{32}. No response.	Shimkin 1955 (two)
—	—	P^{32}. Good response.	Wintrobe 1954
7	—	Folic acid antagonists. No useful response.	Burchenal 1949
10	—	Folic acid antagonists. No useful response.	Burchenal 1951
3	—	Folic acid antagonists. No response.	Medal 1953
3	—	Folic acid antagonists. No response.	Sanchez 1953
—	—	Folic acid antagonists. No response.	Shimkin 1955 (two)
1	—	Folic acid antagonists. No response.	Soto 1952
3	1	Folic acid antagonists and citrovorum factor. Some hematological response.	Spigliati 1953
—	—	Folic acid antagonists. Of little value.	Wilkinson 1953
—	—	Folic acid antagonists. Contraindicated.	Wintrobe 1954

No. of Cases	*No. Responding*	*Comments on Therapy*	*References*
7	4	Folic acid antagonists. 1 Complete rem. for 7 mos.	Wright 1950
4	4	Ethyleneimines. Good remissions with E39.	Consoli 1957
2	2	Ethyleneimines. Brief remissions with E39.	DiPietro 1957
4	4	Ethyleneimines. Some remissions.	DiPietro 1952
8	3	Ethyleneimines. Fair remissions with 9500.	Paterson 1951
1	1	Ethyleneimines. Fair remissions with 9500.	Paterson 1953
1	1	Ethyleneimines. Fair remissions with 7924.	Paterson 1953
3	1	Ethyleneimines. Fair remissions with E39.	Rosa 1955
1	1	Ethyleneimines. Good response with E39.	Verga 1957
9	8	Phenylbutazone. Brief but good remissions.	Alcozer 1956
20	11	Phenylbutazone. Clinical response.	Bichel 1956 (1)
20	11	Phenylbutazone. Clinical response.	Bichel 1956 (2)
1	1	Phenylbutazone. Brief clinical response.	Boen 1956
1	1	Phenylbutazone. Excellent remission for 11 mos.	Deshmukh 1956
10	10	Phenylbutazone. Fair remissions.	Gilsanz 1955
—	—	Phenylbutazone. Some clinical improvement.	Heilmeyer 1953
—	—	Myleran. Some rems. in 29 cases of H.D., leukemia.	Emich 1955
17	17	Myleran. 10 Very good, 7 good responses.	Klima 1954
1	1	Myleran. Clinical improvement.	Krauss 1951
10	—	Myleran. Some good responses.	Marmont 1954
35	23	Myleran. Clinical improvements.	Rottino 1954
—	—	Myleran. No response.	Wintrobe 1954
24	—	Urethan and x-rays. Good rems.	Bock 1950
1	—	Urethan and x-rays. No response.	Cervini 1949
8	4	Urethan and x-rays. Brief rems. and 1 case contraindicated.	Cifarelli 1949
—	—	Urethan and x-rays. Poor response.	Fritze 1950
—	—	Urethan and x-rays. Poor response.	Wilkinson 1953
—	—	Urethan and x-rays. No response.	Wintrobe 1954
5	—	6-MP. No response.	Burchenal 1953
—	—	6-MP. No response.	Burchenal 1954
4	—	6-MP. No response.	Gaffney 1954
1	—	6-MP. Giant cell formation.	Sansone 1954
—	—	6-MP. Contraindicated.	Wintrobe 1954

No. of Cases	*No. Responding*	*Comments on Therapy*	*References*
1	1	As^{76}. Effective.	Mallet 1950
1	—	As^{76}. Poor response.	Mallet 1951
2	2	As^{76}. One case in complete remission after 15 mos.	Mallet 1952
2	2	As^{76}. 1 Complete rem. after 5 mos., 1 good remission.	Marchal 1951
—	—	As^{76}. Some response.	Marchal 1952 (1)
2	2	As^{76}. 1 Complete, 1 partial remission.	Marchal 1952 (2)
4	4	As^{76}. Too little isotope to evaluate but 2 mos. rem.	Block 1949
2	2	Au^{198}. Good remissions.	Hohl 1954
1	1	Au^{198}. Complete remission.	Muller 1951
—	—	Au^{198}. Some remission.	Riordan 1953
—	—	Au^{198}. Fair response.	Werff 1955
8	8	Bi^{206}. Complete remissions.	Werff 1956
—	—	Sulfur mustards. Similar response as HN2.	Alpert 1957
1	1	Mitomen. Some remission.	Apel 1957
1	1	Mechlorethamine, oxytetracycline. Good rem.	Ariel 1957
—	—	Animal protein factor, antibiotics. Good rem.	Barnard 1953
13	11	NaF, iodoacetic acid, malonic acid, Na, azide. 7 Good, 3 fair objective rems., 7 good, 4 fair subjective responses.	Black 1949
1	1	Testosterone, amino acids. Rem. for 15 months.	Brocq 1949
15	4	Fungi extracts. Survival for 12 mos.	Cantero 1951
8	4	Phenylalanine. 3 Good, 1 partial rem.	Consoli 1956
1	1	Vitamin D. A good adjunct to x-rays. Good rem.	Desmonts 1951 (1)
3	3	Vitamin D. Good blood picture to 30 months.	Desmonts 1951 (2)
2	2	Chloramphenicol. Fair response.	Desmonts 1954
5	2	Oligocene metals. Complete rem.	Dubois-Ferriere '51-'53
19	12 *	Azaserine. Clinical response.	Ellison 1954
6	6	Cilag 61, x-rays. Good remissions.	Fiedler 1955
2	—	Splenectomy. No benefit.	Fisher 1951
2	—	Splenectomy. No benefit.	Fisher 1952
—	—	Orthobiotic serum. No response.	Gate 1950
—	—	Diet. Some response.	Gerson 1954
1	—	Diamox. Renal lesions developed.	Glushien 1956
6	—	Alpha-peltation. Brief remissions.	Greenspan 1954
1	1	Ferro-lecithin. Good but brief response.	Heinen 1951

No. of Cases	*No. Responding*	*Comments on Therapy*	*References*
3	—	Butalidon. Some response.	Jeschal 1956
—	—	Chloroquine. Some response.	Jones 1957
21	—	Duamin. Clinical and hematologic remission.	Khazanov 1951
1	1	Irgapycin. Clinical response.	Krauss 1951
78	27	Mechlorethamine. 5 Year survivals for 27 cases.	Levinson 1957
1	—	Arsenic. No response.	Maggi 1950
1	1	Plant extracts. Palliative effect.	Meyer 1950
19	17	Hormones (HBF386, Pancortex) x-rays. 7 Good, 10 fair remissions.	Meythaler 1952
—	—	ACS serum. Some response.	Moya 1953
2	—	$Na_2S_2O_3$. Contraindicated.	Paolino 1952
7	3	SM-1. Good remissions.	Petrakis 1957
2	2	Sb. Good responses.	Piorkowski 1956
5	5	Supernates. Injections caused good response.	Rose 1955
6	3	Trimethylmelamine. Good remissions.	Schmidt 1955
—	—	Hormones (HBF 386), x-rays. Reduces x-ray dose.	Schulte 1952
—	—	Hormones (HBF 386), x-rays. Reduces x-ray dose.	Schulte 1953
34	34	Hormones, FAA. Survivals 6 mos. to 6 years.	Schweisguth 1955
6	1	Azaguanin, flavius hydroxide, FAA. No effect.	Steinfeld 1954
1	1	Sex hormones. Some response.	Storti 1951
5	—	Azaguinin. No effect.	Straus 1950
5	—	Splenectomy. Contraindicated.	Sykes 1954
1	1	Splenectomy. Complete remission.	Whitelaw 1957
2	2	Guanazola. 1 Rem. for 6 weeks, 1 well after 2 years.	Wright 1952
8	—	Sarcolysin. Some remissions.	Consoli 1956
1	—	Carzinophilin. Autopsy showed some benefit.	Shimada 1955
4	—	Methyltestosterone. 2 Severe, 2 mild reactions.	Shanbrom 1957

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SELECTED ABSTRACTS

Antihypertensive Effects of Reserpine in Sustained-Release Form. Grahn, H. V. *J. Am. Geriat. Soc. 6*:671 (1958). In an effort to reduce the side effects from therapeutic measures used in the treatment of mild or moderate essential hypertension, the author used a sustained-release form of reserpine. Previous experience with reserpine had produced side effects such as pruritus, depression, drowsiness, nasal stuffiness, gastric distress, and dizziness which were as distressing to the patient as the symptoms of the disease. Patient cooperation in taking the drug was frequently difficult to obtain.

Fifty-five patients were included in the study. Twenty-eight patients (Group A) were fom 19 to 59 years of age, and 27 patients (Group B) were from 60 to 91 years of age. Most of the patients were tense, nervous persons who felt that they were under great pressure either in their occupations or at home. The average pre-treatment blood pressure in Group A was 183/104, and in Group B it was 193/104.

In 49 patients, the initial dosage was one 0.5 mg. sustained-release capsule daily. In six patients, the initial therapy was a single dose of reserpine intramuscularly followed by 0.5 mg. as a sustained release capsule. After a week to ten days, dosage was changed to maintenance levels based upon the patient's response to therapy. Most patients were maintained on one 0.25 mg. sustained-release capsule daily. A few required two capsules or a single 0.5 mg. capsule daily.

The average systolic blood pressure in Group A was reduced by 33 mm. Hg, and the diastolic by 23 mm. In the geriatric patients (Group B), the average reductions were 37 mm. systolic and 16 mm. diastolic. Seventy-five per cent of the patients in Group A and 82 per cent of those in Group B achieved normotensive diastolic blood pressures. Side effects were evident in a few cases but drowsiness in 4 patients and occasional nasal congestion in one patient were the only side effects that persisted with maintenance dosage levels. In no case were they sufficiently severe to require discontinuation of therapy.

The author concluded that reserpine in sustained-release form reduced the incidence of side effects and provided more uniform relief from symptoms throughout the day than did reserpine in conventional form. It was also found to be equally effective in geriatric and non-geriatric patients.

The Oral Treatment of Pernicious Anemia With a Vitamin B_{12} Peptide. Heathcote, J. G., and Mooney, F. S. *Lancet 1*:982 (1958). The long accepted concept of the requirement of an intrinsic factor for the utilization of vitamin B_{12} has been brought into question by the authors. They noted that this intrinsic factor has never been isolated and they doubt its existence. Rather, they feel that the fundamental cause of pernicious anemia is an inability to absorb vitamin B_{12} due to the failure of simple proteolysis in the stomach as a result of the absence or inadequate secretion of gastric juice. For absorption they feel that the vitamin must be in the form of a simple peptide complex of low molecular weight, dialysable and assimilable by microorganisms. Thus, combined vitamin B_{12} in food must first be digested and then the pure crystalline vitamin combined with a peptide before absorption in the intestine can occur.

In order to test this hypothesis, the authors combined vitamin B_{12} with a peptide to form a complex (H. P. P.) by fermentation with Streptomyces. The complex was dialysable and ultrafiltrable through Cellophane and collodion membranes. This preparation was described as producing the most effective clinical results of any oral preparation yet known, in the treatment of pernicious anemia.

Six newly diagnosed cases of pernicious anemia were treated exclusively with this preparation. A good hematological and clinical response was evident in each case, which was maintained for 140 to 290 days. A reticulocyte crisis consistently developed at the end of the first week and no case developed signs of cord deterioration. A seventh case, which showed early subacute combined degeneration of the cord following treatment with another oral preparation, responded promptly to treatment with H. P. P. with an amelioration of the symptoms and subjective improvement.

The Absorption of Drugs From the Small Intestine of the Rat. Schanker, L. S., Tocco, D. J., Brodie, B. B. and Hogben, C. A. M. *J. Pharmacol. 123*:81 (1958). The relative rates of absorption of a large number of drugs were measured by perfusing solutions of the drugs through the entire length of the small intestine of the anesthetised rat. Where the rate of absorption was rapid, a single perfusion gave sufficient data for evaluation. Other drugs, which were slowly absorbed, were studied after continuous perfusion for three hours.

The authors found no evidence for the existence of specific transport mechanisms and concluded, therefore, that absorption of drugs is a passive physical process. A relationship between the dissociation constant and the degree of absorption of compounds of widely different chemical structure was observed. Acidic drugs were found to be rapidly absorbed if their pKa values were greater than three. Basic drugs were rapidly absorbed if their pKa values were less than eight. The stronger acids and bases were relatively slowly absorbed and the absorption of very strong acids and bases was imperceptible.

The authors concluded that the absorption of drugs from the intestine of the rat can best be explained by assuming a simple diffusion of unionized drug across a barrier which may be lipoid in nature.

The Treatment of Peptic Ulcers With an Anticholinergic and Tranquilizers. Winkelstein, A. *Am. J. Gastroenterology* (*30*:68 (1958)). Because emotional stress, manifested by tension and anxiety, is believed a major predisposing or precipitating factor in peptic ulcer formation, gastroenterologists frequently prescribe sedatives or tranquilizers along with anticholinergics to modify the patient's response to stress. Although reserpine is sometimes prescribed for patients with gastrointestinal diseases, there is some evidence that reserpine increases gastric acidity and, therefore, may be contraindicated in patients with peptic ulcer or a history of this disease.

The author administered diphenmethanil methylsulfate (Prantal) and reserpine to 144 patients and diphenmethanil methylsulfate and perphenazine (Trilafon) to 95 patients. Improvement was observed in all but 6 of the patients after one month of therapy with either combination. Radiographic studies were made in ten patients with duodenal ulcers and in 15 patients with gastric ulcers before and after one month of treatment. Thirteen of the fifteen patients who received diphenmethanil methylsulfate and perphenazine and six of the ten patients who received diphenmethanil methylsulfate and reserpine showed evidence of healing.

The author concluded that the combination of diphenmethanil methylsulfate and perphenazine was preferred to the combination of diphenmethanil methylsulfate and reserpine. The two combinations were essentially equal in their ability to control emotional factors but the former has little or no risk of increasing gastric acidity.

BOOK REVIEWS

Symposium on Protein Structure. Edited by Albert Neuberger. 351 pp. John Wiley & Sons, Inc., New York, N. Y., 1958. Price: $7.75.

This is a collection of the main papers presented at the 1957 Symposium on Protein Structure held under the auspices of the Biological Chemistry Section of the International Union of Pure and Applied Chemistry. The book covers the fields in which the main progress in protein chemistry might occur; however, certain aspects such as the physical chemistry of proteins have been excluded.

There are 18 sections of which three are written in German; four, in French; and the remaining eleven, in English. The sections deal with general problems and methods, specific proteins (hemoglobin and myoglobin), proteolytic enzymes, ribonuclease, other proteins, and peptides. There is a subject index at the end of the book which serves as a rapid guide for checking on details included throughout the papers.

The book is an excellent presentation of protein biochemistry presented in a most competent and efficient manner.

BERNARD WITLIN

Educating Spastic Children. F. Eleanor Schonell. 242 pp. Philosophical Library, New York 16, N. Y. Price: $6.00.

For those persons working with the handicapped, this book will be informative and stimulating. It will be helpful to the lay public seeking information about spastic children and what can be done for these children.

Dr. Schonell presents the results of an extensive survey made in the United States, Canada, and New Zealand and her work in Queensland and close contact with other Australian spastic centers.

It is the study of the results observed from this disabling disease and what has been accomplished in the rehabilitation of these affected persons.

J. I. FEINMAN

Progress in Medical Virology. E. Berger and J. L. Melnick, Editors. 304 pp. Hafner Publishing Co., New York, N. Y., 1958. Price: $11.50.

This is the first attempt to make available an annual review of medical virology. The book was edited by two well-known virologists and contains sections written by one of the editors and eleven collaborators of international repute. Included are the etiologic, epidemiologic, diagnostic, and laboratory aspects of the viral diseases considered.

The preface is repeated three times—once each in English, French, and German. However, the text, which is a reprinted compilation of selections previously printed by the publisher, is completely in English. The papers selected are indexed and bound as the "Annual Review" and cover: nucleic acid as the carrier of viral activity, viral carrier state in tissue culture, enteroviruses, Coxsackie infections of the newborn, poliovirus vaccine production, influenza virus, Spring-Summer encephalitis, Kyasanur Forest disease, and antibody flocculation reactions.

The book should prove useful to those interested in the field of virology.

BERNARD WITLIN

Notes on Atomic Energy for Medical Officers. Staff of the British Royal Naval Medical School. v + 169 pp. Philosophical Library, Inc., New York 16, N. Y., 1956. Price: $4.75.

The intent of the book is to present the basic knowledge necessary to understand both the short- and long-term effects of atomic explosions as well as the dangers presented by other military uses of atomic energy. The first nine chapters are devoted to basic topics in nuclear physics and the next five chapters to the effects of radiation on living tissue, an evaluation of the hazards, and the treatment of casualties. Monitoring instruments and radiation protection are considered in the last two chapters. The manner of presentation permits the reader to acquire a thorough understanding of the subject matter with only a modest background in physics and biology.

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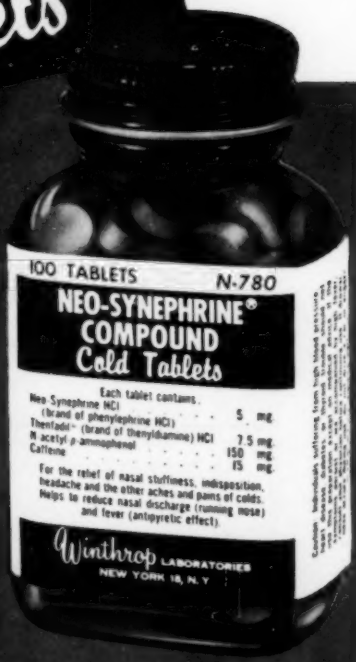

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